

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Previously presented) A method of preparing DNA fragments from a sample of nucleic acids to be analyzed, which method comprises selectively fragmenting the nucleic acids by means of at least the following steps:

I. for a first selection of short fragments:

- a) preparing first double-stranded DNA fragments F1 using at least one restriction enzyme E1 capable of randomly fragmenting the sample of nucleic acids to be analyzed, and generating said DNA fragments F1 with blunt or cohesive ends;
- b) ligating the ends of said DNA fragments F1 obtained in step a) to at least one adapter AA', so as to form a unit – located at the junction of the complementary end of said adapter and of the 5' end of said fragments F1, such that:  
  
the sequence of said unit is that of the first N-x base pairs of the recognition site - comprising N base pairs – of a restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, with  $1 \leq x \leq N-1$ , and  
  
its 3' end – located 5' of said DNA fragments F1 – is that of the restriction site of the E1 restriction enzyme, so as to obtain DNA fragments F'1;
- c) cleaving the DNA fragments F'1 obtained in b) in the vicinity of their 5' end using said restriction enzyme E2, so as to select a fraction of short fragments F2;
- d) purifying said fraction of short fragments F2, and optionally

II. for a second selection of one or more subset(s) of fragments from the fraction of short

fragments from the fraction of short fragments F2 obtained in step d):

- e) ligating the free end (not linked to the adapter AA') of short fragments F2 obtained in d) to at least a second complementary adapter BB' (production of fragments F'2); and
- f) amplifying the short fragments F'2 linked to said adapters (AA' and BB'), using at least one pair of primers, at least one being optionally labeled at its 5' end, so as to select at least one subset of short fragments F'2 from the fraction of short fragments F'2 obtained in d).

2. (Previously presented) The method as claimed in claim 1, wherein step a) is carried out with two different E1 restriction enzymes, E1<sub>A</sub> and E1<sub>C</sub>, such that:

at least one generates cohesive ends, different from those optionally generated by the other restriction enzyme, and  
the 3' end of E1<sub>A</sub> restriction site is that of the unit as defined in step b).

3. (Previously presented) The method as claimed in claim 2, wherein one of the enzymes cleaves frequently and the other rarely.

4. (Previously presented) The method as claimed in claim 3, wherein:  
the enzyme that cleaves frequently is the enzyme E1<sub>A</sub>, which enzyme E1<sub>A</sub> generates at least one end of a fragment F1 that binds to the adapter AA' in step b), and  
the enzyme that cleaves rarely, is the enzyme E1<sub>C</sub> which generates at least one end of a fragment F1, which binds, in step b), to a second adapter CC' that is different from the

adapter AA'.

5. (Previously presented) The method as claimed in claim 1, wherein steps a) and b) are carried out simultaneously.

6. (Previously presented) The method as claimed in claim 1, which further comprises purifying the fragments less than 1000 bp, prior to the ligation step b).

7. (Previously presented) The method as claimed in claim 1, wherein the adapter AA' as defined in step b) comprises, at the 3' end of the strand A or 5' end of the strand A', or both, a zone 1 of approximately 1 to 8 bases or base pairs, which is partially or completely identical or complementary to the restriction site of the enzyme E1, which zone 1 is chosen so as to reconstitute the sequence of the first N-x bases or base pairs of the recognition site of the restriction enzyme E2, by ligation of said adapter AA' to the ends of said DNA fragments obtained in a).

8. (Previously presented) The method as claimed in claim 7, wherein zone 1 includes one or more mismatches with the sequence of said cleavage site of the restriction enzyme E1.

9. (Previously presented) The method as claimed in claim 1, wherein the adapter as defined in step b) comprises, upstream of the zone 1, a zone 2 of at least 6 base pairs.

10. (Previously presented) The method as claimed in claim 1, wherein the adapter as defined in step b) comprises at least one base located between the zone 1 and the zone 2, different from that which, in the cleavage site of the restriction enzyme E1, is immediately adjacent to the complementary sequence corresponding to the zone 1.

11. (Previously presented) The method as claimed in claim 1, wherein the adapter as defined in step b) comprises a phosphate residue covalently linked to the 5' end of the strand A'.

12. (Previously presented) The method as claimed in claim 1, wherein, when said method consists of a single selection of short fragments according to steps a) to d), it comprises at least one additional step b'), c') or d') or a combination thereof comprising amplifying the fragments F'1 or F2 using a pair of primers.

13. (Previously presented) The method as claimed in claim 1, wherein the adapter AA' as defined in step b) is linked, at the 5' end of its strand A, to a label.

14. (Previously presented) The method as claimed in claim 1, wherein the 5' end of the strand C' of the adapter CC' is linked to a label, which label is attachable to a functionalized solid support.

15. (Previously presented) The method as claimed in claim 12, wherein the fragments F'1 obtained in step b) or b') are brought into contact with said functionalized support prior to the cleavage step c), and the fraction of short fragments F2 of step d) corresponds to the fraction of fragments that is either retained on said support (adapter AA' linked to the label that attaches to the support) or free (adapter CC' linked to the label that attaches to the support).

16. (Previously presented) The method as claimed in claim 13, which comprises, in step e), ligating several different complementary adapters, each comprising, at the end of 5' end of the strand B or at the 3' end of the strand B', a specific sequence of 1 to 10 bases.

17. (Previously presented) The method as claimed in claim 13, wherein said adapter BB' as defined in step e) comprises a phosphate residue covalently linked to the 5' end of the strand B.

18. (Previously presented) The method as claimed in claim 13, wherein one of the primers as defined in step f) is linked, at its 5' end, to an appropriate label.

19. (Previously presented) The method as claimed in claim 1, which comprises an additional step d') or g) comprising obtaining single-stranded fragments from the short fragments F2 obtained in step d) or d') or else from the short fragments F'2 obtained in step f).

20. (Previously presented) The method as claimed in claim 1, which further comprises purifying the amplification products obtained in step b'), c'), d') or f) or of the single-stranded fragments obtained in step d') or g).

21. (Previously presented) A short DNA fragment, representing a genetic marker, obtained by the method as claimed in claim 1, which has a sequence of less than 100 bases or base pairs, comprising at least one specific sequence consisting of a fragment of genomic sequence or of cDNA sequence bordered, respectively, by the recognition site and the cleavage site of a restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, such that the 5' end of said specific sequence corresponds to the last x base pairs of the recognition site – having N base pairs – of said enzyme E2, with  $1 \leq x \leq N-1$ , said marker including, at each end, at least 6 bases or 6 base pairs of nonspecific sequence.

22. (Previously presented) The DNA fragment as claimed in claim 21, which is a single-stranded fragment.

23. (Previously presented) The DNA fragment as claimed in claim 21 which is linked, at one of its 5' ends, to an appropriate label.

24. (Previously presented) A DNA chip, characterized in that it comprises a DNA fragment as claimed in claim 21.

25. (Cancelled).

26. (Cancelled).

27. (Previously presented) A method of hybridizing nucleic acids, which comprises hybridizing the nucleic acids with a DNA fragment as claimed in claim 21.

28. (Previously presented) A kit for carrying out the method of claim 27.

29. (Cancelled).

30. (Cancelled).

31. (Previously presented) A kit for carrying out the method as claimed in claim 1, which comprises at least one adapter AA' as defined in claim 7, and a restriction enzyme E2 as defined in claim 1.

32. (Previously presented) The kit as claimed in claim 31, which further comprises at least one adapter BB' as defined in claim 1, and a pair of primers as defined in claim 1.

33. (Previously presented) The kit is claimed in claim 28, which comprises at least one DNA fragment as claimed in claim 21.

34. (Previously presented) The kit as claimed in claim 28, which comprises at least one DNA chip as claimed in claim 24.

35. (Previously presented) The kit as claimed in claim 33, which further comprises an oligonucleotide probe complimentary to the DNA fragment.

36. (Previously presented) A method of hybridizing nucleic acids, which comprises hybridizing the nucleic acids with a DNA chip as claimed in claim 24.

37. (Previously presented) The method as claimed in claim 12, wherein the pair of primers are a pair of labeled primers.

38. (Previously presented) The method as claimed in claim 13, wherein the label is a label for detecting nucleic acid hybrids.

39. (Previously presented) The method as claimed in claim 13, wherein the label is attachable to a functionalized solid support.